REMARKS

In paragraph 4, on page 2 of the Office Action, the Examiner rejects Claims 1-10 and 12-17 under 35 U.S.C. § 112, first paragraph.

Specifically, the Examiner states that the specification does not provide support for the expression "duration of time".

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

The specification teaches culturing $CD34^+$ cells in the presence of Flt3-ligand for approximately 2 weeks (Examples 1 and 2) and daily over a period of 19 days (Example 3).

In view of the amendment to the claims to limit the duration to "a period of 14 to 19 days", this rejection is deemed moot

In paragraph 6, on page 4 of the Office Action, the Examiner rejects the pending claims under 35 U.S.C. § 103 as being unpatentable over Lyman et al in view of Elliott et al, Srivastava et al and Brem et al for the reasons of record.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

In view of the amendment to the claims to limit the duration to "a period of 14 to 19 days", this rejection is deemed moot. None of the cited art, alone or in combination teach or suggest such an administration duration.

As previously argued, Lyman et al teaches a method for expanding hematopoietic stem and progenitor cells (see column 26, lines 23-37 thereof). The stem cells were cultured for 4 days (96 hours plus 24 hours with radioactive tag) and

cultured an additional 2 days in the presence of flt3-ligand. This is an approximate culture time of 6 days for expanding hematopoietic stem and/or progenitor cells.

In contrast, Examples 1-2 of the present application describe culture conditions for generating large numbers of dendritic cells. Examples 1-2 describe culturing CD34+ cells in the presence of flt3-ligand for approximately 2 weeks and Example 3 shows administering flt3-ligand daily over a period of 19 days.

Thus, the hematopoietic stem and/or progenitor cells must be exposed to flt3-ligand for an extended period in order to generate an increase in the number of dendritic cells in the patient. This feature is not taught or suggested in any other references cited by the Examiner. There is clearly no motivation in the art to achieved the claimed invention, and thus the Examiner has failed to establish a *prima facie* case of obviousness.

The Examiner further contends that the prior art teaches that GM-CSF can eliminate tumor cells in combination with other chemotherapeutic agents, such as cytokines (Brem et al); and recognizes the advantages of providing stimulation to various compartments of the recipient to maximize the physiological and therapeutic response (see Elliot et al, Srivastava and Brem et al), thereby providing the motivation to combine the Flt3-ligand of Lyman et al with the GM-CSF of Elliot et al, Srivastava and Brem et al, to achieve the present invention.

It is Applicants understanding that the Examiner feels that although the art does not suggest making the claimed combination in order to increase dendritic cells, it does suggest making the

claimed combination in order to treat tumor cells, and thus the rejection is proper.

The Examiner previously failed to appreciate that even if there is motivation in the art to combine the references to reduce tumor formation and/or to augment a tumor-specific immune response, there is no motivation to increase the number of dendritic cells. In any event, evidence of "unexpectedly superior results" as previously provided to the Examiner, is legally sufficient to rebut a *prima facie* case of the obviousness.

It is also Applicants understanding that the Examiner alleges that if there is any motivation, than it does not matter if there are "unexpected" results.

Applicants respectfully submit that the Examiner's position is legally incorrect.

As set forth at MPEP §2142, the question of obviousness requires that the Examiner first establish a *prima facie* case of obviousness, and then consider any evidence of non-obviousness that Applicants may have to rebut that *prima facie* case.

As has been asserted in the present application, and as discussed above, the present invention gives rise to unexpected effect in the treatment of cancer, and such is evidence that the presently claimed method are non-obvious. The Examiner is requested to appropriately consider the following law.

In the case of *In re Papesch*, 137 USPQ 43 (CCPA 1963), the Examiner took the following position, analogous to the position taken by the Examiner in the present case:

> Such contribution may properly be protected by claims to the mode of employing the compounds for their unexpected novel use, but does not support claims

> covering compounds which are structurally obvious and which also exhibit a family of properties and characteristics common to, and not differing significantly from, those of the homologue known and available in the prior art. ***An unexpected difference in a single property should not be adequate to support a claim for a novel, but obvious, homologue….*** Id. at page 46 (emphasis added).

However, both the Board and the Court found otherwise:

> As to the Examiner's view that in a case such as this the applicant should claim his invention as a process utilizing the newly discovered property, the board appears to have ignored it, properly we think. ***It is contrary to practically all of the above decisions wherein no fault was found with granting product claims.*** Id. at page 52 (emphasis added).

This law was strengthened by the CCPAs subsequent decision in *In re McLamore*, 154 USPQ 114 (CCPA 1967):

> We there faced virtually the same argument the board is posing, however, and rejected it, namely, that under such a state of facts the invention should not be claimed as a compound but by some form of claim reciting properties, such as the method of lowering blood sugar…. See the last four paragraphs of our opinion wherein we stated ***we had also faced the same question in In re Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43, and answering it by approving claims to the compounds.*** Id at 117.

The Federal Circuit has continued to endorse this reasoning. For example, in *In re Chupp*, 2 USPQ2d 1437 (Fed. Cir 1987), the Board took a position similar to the Examiner's position in the instant case:

> The board held that because the claims were limited to no particular weed or crop, 'the showing is not fairly representative of that which is encompassed by the claims.' Therefore,

> concluded the board, the evidence of superiority in corn and soybeans could not rebut the *prima facie* obviousness of the 'invention as a whole.' Id at 1439.

The Federal Circuit's response:

> ***Papesch held that a compound can be patented on the basis of its properties; it did not hold that those properties must produce superior results in every environment in which the compound may be used.*** To be patentable, a compound need not excel over prior art compounds in all common properties. Evidence that a compound is unexpectedly superior in one of a spectrum of common properties, as here, can be enough to rebut a *prima facie* case of obviousness. Id at 1439 (emphasis added).

Also see *Knoll Pharmaceutical Co. v. Teva USA Inc.*, 70 USPQ2d 1957 (Fed. Cir. 2004) and *Richardson-Vicks Inc. v. Upjohn Co.*, 44 USPQ2d 1181 (Fed. Cir. 1997), applying the law of unexpected properties to pharmaceutical composition and process claims alike, and finding no distinction as to the relevance of unexpected properties for a particular type of claim.

Therefore, under the controlling law, Applicants' unexpected properties are relevant to the non-obviousness of the presently invention, and this evidence must be considered by the Examiner. That is, the Examiner must determine whether Applicants' unexpected properties are sufficient to rebut a *prima facie* case of obviousness, which again, Applicants submit has not even been raised.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested in Lyman et al and that the combination thereof with Elliot et al, Srivastava et al and Brem et al does not give rise to the present invention. In

any event, Applicants data is sufficient to rebut any *prima facie* case of obviousness the Examiner might have raised. Thus, Applicants request withdrawal of the Examiner's rejection.

In view of the amendments to the claims and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at the below-listed number on any matters which might arise.

Respectfully submitted,

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